Supporting Statement A for

Evaluation of Risk Factors Associated with HIV, HBV and HCV in Chinese Donors (NHLBI)

October 21, 2008

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SUPPORTING STATEMENT

A. Justification

A.1. Circumstances Making the Collection of Information Necessary

Understanding the risk factors associated with HIV, HBV and HCV infections in donors is essential for developing donor behavioral screening policies. Injection drug use, sexual transmissions, transfusion history, and medical injections are thought to be major routes of transmission in China but their relative importance in blood donors is unknown.

In the U.S., risk factors have been better characterized for these infections but, questions still remain. Risk factors cannot be identified in 33% and 40% of persons with acute hepatitis B and C respectively, and risk factors may differ between the U.S. and China. For example, we may be able to assess whether treatments commonly used in China, such as acupuncture and medical injections, are important routes of HBV and HCV transmission.

The primary objectives of the proposed studies are to assess:

- the primary risk factors associated with HIV, HBV and HCV in China.
- the relative importance of injection drug use, heterosexual transmission, family history, transfusion history, history of previous whole blood or plasma donation, male to male sex, medical injections, acupuncture, and tattoos as routes of transmission for HIV, HBV and HCV in China.
- other important routes of transmission for these viruses such as sex with an injection drug user, snorting drugs, living with someone who has HBV and HCV, living with someone who injects drugs, sharing a toothbrush or a razor, having been in jail, occupational history, having surgery, etc. in China

It is proposed to conduct a large, multi blood center case-control study to meet the study objectives. For the HIV protocol, cases will be donors with confirmed anti-HIV antibody reactivity. The control group will include randomly-selected HIV non reactive donors matched by blood center and fixed versus mobile donation sites. Consented donors will be interviewed by trained staff using the RFQ. The location for this activity can be either at the local C-CDC office or blood center. Blood Centers will contact potential Controls by phone and/or mail, inviting them to come back to participate in this study. Controls will be consented and interviewed using the same RFQ by C-CDC or blood center staff, either at the local C-CDC or blood center.

The second protocol assessing risk factors related to HBV and HCV will have three groups of donors: “HBV Group”: HBV (HBsAg) positive donors either from prescreening (rapid testing) or routine screening testing. Confirmatory testing for HBV will be done for these donors. “HVC Group”: HCV (anti-HCV) positive donors from routine screening testing (blood centers do not do prescreening rapid testing for anti-HCV). Confirmatory testing for HCV will be done for these donors. The third group will be a “Control Group” including donors with negative results for all prescreening and routine screening tests. No additional testing is done for these donors. Donors in all three groups will be mailed a Risk Factor Survey study packet. The packet will include a study information sheet (discussing the purpose and nature of this study), an informed consent document explaining the voluntary nature, the benefits and risks of this study, a Risk Factor Questionnaire, and an envelope with paid postage for the donor to mail their completed questionnaire back to the blood center.

Section 301 of the Public Health Service Act - 42 U.S.C. 241 authorizes the Secretary of Health and Human Services to conduct in the Public Health Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnoses, treatment, control, and prevention

of physical and mental diseases and impairments of man. This authority has been delegated to the NIH Director, and, in turn, further delegated to the Institute Directors, subject to certain limitations which do not generally apply here.

22 U.S.C. 2101 and 22 U.S.C. 2102 (See Attachment 5) authorize the Secretary, in carrying out his authority under any provision of law to conduct and support health research and research training, to make such use of health research and research training resources in participating foreign countries as he may deem necessary and desirable. This statutory provision may be read to authorize awards to foreign institutions under statutory provisions that authorize the Secretary to support health research and research training, such as 42 U.S.C. 241. This authority has been delegated to the NIH Director, and, in turn, further delegated to the Institute Directors, subject to certain limitations which do not generally apply here.

A.2. Purpose and use of the information

Since 1989, the NHLBI-sponsored Retrovirus Epidemiology Donor Study (REDS) program has conducted epidemiologic, laboratory and survey research in the field of blood safety. In 2006, the REDS-II program initiated an international component, extending the scope of blood safety research to include investigators in Brazil and China. The goal of the REDS-II International Component is to conduct epidemiologic, laboratory, and survey research on blood donors in selected resource-limited countries in regions seriously affected by the AIDS epidemic to help increase the safety and availability of blood for transfusion. Specific objectives for REDS-II International are to 1) assess and monitor the prevalence and incidence of HIV-1, HIV-2, and other existing as well as newly discovered infectious agents that pose a threat to blood safety, 2) assess risks of transfusion –transmitted infections, 3) assess the impact of existing and new blood donor screening methodologies on blood safety and availability, 4) evaluate characteristics and behaviors of blood donors including risk factors for acquiring HIV and other blood-borne agents, and 5) evaluate the donation process for ways to improve the safety and adequacy of the blood supply, and reduce infectious disease burden.

Data collected in this study will be of practical use to the blood banking community. In addition to the traditional route of peer reviewed scientific publication, previous REDS-I study data were the subject of numerous requested presentations by Federal and non-Federal agencies, including the FDA Blood Products Advisory Committee, the HHS Advisory committee on Blood Safety and Availability, the Americas Blood Centers Association (AABB) Transfusion-Transmitted Diseases Committee, and the Americas Blood Centers Association. We anticipate similar requests for data generated from this study.

A.3. Use of Information Technology and Burden Reduction

For HIV study, all respondents will be invited to return to the blood center or C-CDC where the survey will be administered by a trained interviewer. Donors participating in the HBV/HCV protocol will be given an option to complete the paper survey and mail it back or to use a web based survey tool to submit their responses. Both the protocols use a survey instrument with the same set of questions but a different cover sheet. (See Attachment 1.1 and 1.2)

A.4. Efforts to Identify Duplication and Use of Similar Information

There is evidence of similar research in other social groups such as sex workers in China but no research has been previously conducted to study viral risk factors in Chinese Blood Donors.

A.5. Impact on Small Businesses or Other Small Entities

Small businesses or entities are not involved. All respondents are individual blood donors.

A.6. Consequences of Collecting the Information Less Frequently

Questionnaires will be administered only once to all subjects in a paper format for both the HIV and HBV/HCV studies. The same Risk Factor Questionnaire (RFQ) will be used to assess risk factors for HIV, HCV, and HBV infections. The questionnaire will collect general demographic and risk factor information pertinent to all three viruses (HIV, HCV, and HBV).

Donors participating in the HBV/HCV study will also have an option to complete the survey on secure internet website.

A.7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The proposed data collection is consistent with 5 CFR 1320.5.

A.8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency

The 60-day Federal Register Notice was published on July 31, 2008. One comment was received and responded via email by the Project Officer. There has been consultation outside of NHLBI to conceptualize and design the proposed study. The final study design was developed, reviewed, and approved by the REDS-II subcommittee, the REDS-II Steering Committee, and the Observational Study Monitoring Board (OSMB) (See Attachment 3.1 for a complete list of members). The OSMB reviewed the final protocol and provided input and comments. Revisions were made to the protocol incorporating the suggestions of the OSMB.

A.9. Explanation of Any Payment or Gifts to Respondents

For HBV& HCV Risk Factor study, donors will be given an incentive of about $3 US dollars (or 20 yuan RMB) with the mailed questionnaire. For the HIV study, since the survey is done by in-person individual interview, all respondents will receive a reimbursement of transportation fee to the Blood Center or CDC (about $15 US dollars or 100 yuan RMB). They will also receive a compensation for the time to complete the interview (about $30 US dollars or 200 yuan RMB).

A.10. Assurance of Confidentiality Provided to Respondents

The Privacy Act does not apply to the proposed data collection since identifiable information will not be collected on this questionnaire.

A.11. Justification for Sensitive Questions

The questionnaire has been developed based on a thorough review of the current international and Chinese literature. Efforts have been made to ensure that the questionnaire is

comprehensive and culturally appropriate. The questionnaire has been translated into Chinese and Uyghur languages. The Uyghur translation will be used for Uyghur donors in Urumqi, Xinjiang. We have conducted focus group discussions and cognitive testing to improve the potential reliability of responses. Blood centers will mail a study enrollment packet to all donors selected as potential Cases and Controls. For the HBV/HCV protocol, Cases and Controls will receive the same packets which will include a study information sheet, study questionnaire, a small monetary reward for taking the survey and a pre-posted envelope for returning the completed questionnaire to the blood center. Due to confidentiality concerns, donors will not be asked to sign the consent form. By sending back the completed questionnaire, a donor indicates his/her consent for this study. Our previous experience in conducting small risk factor studies taught us that in the current blood donation setting, achieving trust and providing confidentiality are critical in obtaining accurate risk factor information. Based on our past experience, we believe that the best approach is to allow the donors to complete questionnaires in private and assure the donors of the confidential nature of the investigation.

The purpose of the interview questions is to collect donor profile data for comparing risk exposures between blood donors who test HIV, HBV/HCV positive (cases) and HIV, HBV/HCV negative (controls).

The demographic information collected will include gender, date and place of birth, ethnicity, current occupation, level of education received and marital status. Previous donation history questions will be used to collect data about the frequency of previous donation and the year and type of each blood donation. In China due to the unsanitary illegal blood collection in the early to middle 1990s, the history of plasma donation in the 1990s has been identified by several studies as a major risk factor for HCV infection. So these questions will capture information on the association between previous donation and HBV/HCV infection status.

To determine motivational factors that lead participants to donate blood there are questions related to incentives and motivation. These questions will help understand the donor's

intention to get blood testing through blood donation (test seeking). Blood bank serology testing may be a magnet that attracts people wishing to be tested. We intend to ascertain donor's perceptions/confidence related to viral serology performed by the blood bank as well whether the blood screening serology testing was contributing factor in donating.

Medical history questions will be used to obtain data related to general medical history exposures that could lead to viral transmission, including acupuncture, medical injection, medical surgery, cosmetic surgery, dental cleaning, dental surgery, endoscopies, both life time and exposure in the year before blood donation.

Due to the unsanitary illegal blood collection and transfusion practices in China in the early to middle 1990s, the history of blood transfusion in the 1990s has been identified by several studies as a major risk factor for viral infection. Thus, questions have been included to collect information about previous transfusions.

Previous deferral information will be collected to ascertain if the blood donor has been deferred at the time of the blood donation and the reason for deferral. In China, the blood centers are building up the information system for deferred donors so next time when these donors come to donate, they will be automatically identified. These questions will be useful for understanding the effectiveness of deferral system and the donors' information of deferral.

Previous diagnosis section will ask questions about the donor's previous diagnosis of hepatitis, HIV and sexually transmitted diseases as well as the infectious status of their family members. Drug use questions will be asked to evaluate the influence of illicit drug use on viral infections. The questions include injected and non-injected illegal drugs use and frequency. To ascertain if illegal drugs use including sharing the drug delivery device, which could lead to disease transmission, we also ask the questions about sharing injected drug delivery device.

The sexual lifestyle questionnaire items are used to obtain data related to sexual lifestyle, including the number of sexual partners during the lifetime increases the odds of having a sexual transmitted disease, as well its spread. The sexual history will allow us to determine the most

prevalent sexual patterns for the Chinese blood donors and whether this pattern may or may not be correlated to specific serologic markers. A better understanding of sexual risk factors for HIV and HBV/HCV may allow us to build more accurate questions to improve the donor qualification process. It may also help us to avoid potential discrimination and unnecessary loss of donors if the patterns of viral transmission are not shown to be associated with sexual activity.

Work place exposure questions are included based on the assumption that the donors who work in a health care profession or other social setting that could lead to exposure to blood or other body fluids could be at higher risk for HIV and HBV/HCV acquisition. To obtain data related to rare risk factors for HIV/HBV/HCV infection such as body piercing and tattoo, we ask about ever exposure and also exposure in the year before blood donation.

Questions will be included to determine the notification service provided by the blood center and whether or not the donor is willing to adhere to the advice for further testing and health care. This helps us understand if the notification is effective.

A.12. Estimates of Burden Hour Including Annualized Hourly Costs

The annualized cost to respondents is estimated at $1940.25 based on $1.50 per hour. It is estimated that each respondent will spend about 20 minutes (0.33 burden hours) to complete the questionnaire. According to China's National Bureau of Statistics in 2006, the average annual wage in China is 21001 Chinese Yuan (or $ 2958 US dollars based on current exchange rate of 1 US dollar = 7.1).

Table A.12-1: Estimated Total Annual Burden Hours

Type of Respondents	Estimated Number of Respondents			Frequency of Response	Average Time per Respondents	Hourly Wage Rate	Respondent Cost
	HIV	Case	350	1	0.33	$1.50	173.25

Blood donors	Risk factor	Control	700	1	0.33	$1.50	346.50
	HBV and HCV Risk factor	Case	1700	1	0.33	$1.50	841.50
		Control	1170	1	0.33	$1.50	579.15
	Total		3920		0.33		1940.25

A.13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

There are no capital or start-up costs, and no maintenance or service cost components to report.

A.14. Annualized Cost to the Federal Government

The annualized cost to the Federal Government for the proposed study is estimated to be approximately $ 240,042 (per year).

A.15. Explanation for Program Changes or Adjustments

This questionnaire constitutes a new collection of information.

A.16. Plans for Tabulation and Publication and Project Time Schedule

The schedule for study activities is shown in Table A.16.

Table A.16: Study Timeline

Activity	Time Schedule
Donor Enrollment	January 2009
Study Completion	December 2011

Subject to NHLBI approval, data will be disseminated to the scientific and blood banking community and others through peer-review journal publications, and presentations at government

(FDA Blood Products Advisory Committee) and professional meetings (American Association of Blood Banks).

A.17. Reason(s) Display of OMB Expiration Date is Inappropriate

The OMB expiration date will be displayed in the upper-right hand corner of the questionnaire.

A.18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification statement of OMB Form 83-I.